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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,821	11/13/2000	Todd M. Kinsella	A-70036/RMS/JJD	9149
959	7590	04/06/2004	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			PONNALURI, PADMASHRI	
			ART UNIT	PAPER NUMBER
			1639	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/712,821	KINSELLA, TODD M.
Examiner	Art Unit	
Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 26 September 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 7-45 is/are pending in the application.
 - 4a) Of the above claim(s) 7-12 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 13-45 is/are rejected.
- 7) Claim(s) 34 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 13 November 2000 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: <u>3/31/04</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Status of Claims

NOTE the previous office action on merits in this application mailed on 6/4/02 in view of the preliminary amendment, which crossed in the mail with the office action has been withdrawn.

1. The preliminary amendment filed on 5/10/02 has canceled claims 1-6, and added new claims 13-37. Amendment filed on 2/5/03 has amended claims 19, 21-22, 24-25, 27, 30-33, and added new claims 38-45. Accordingly claims 7-45 are currently pending in this application.
2. Claims 7-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.
3. The newly added claims 13-45 are being examined in this application. NOTE the restriction requirement (filed on 11/26/02) has been withdrawn and species election has been maintained.
4. Applicant's election without traverse of species of '2a site, IL-4 ε promoter and Renilla mulleri GFP in Paper filed on 9/26/03 is acknowledged.

Priority

5. This application claims priority to provisional application 60/165,189 filed on 11/12/99.
6. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior

nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Drawings

7. The drawings filed on 11/13/00 have been objected. Applicants are requested to see the PTO 948 attached to the previous office action mailed on 6/4/02.

Specification

8. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

9. The attempt to incorporate subject matter into this application by reference to several publications (non-patent literature) and provisional applications is improper because the various publications (e.g., page 15, refers to provisional application) refer to subject matter which is essential to practice the claimed invention. The provisional application in page 15 is referring to several different GFPs used in the claimed method. NOTE the provisional application applicants are relying on is not a priority document of the claimed invention.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 34, 35, 36, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claims recite the specific GFP used in the claimed expression vectors.

The limitations ‘Renilla mulleri GFP’, ‘Ptilosarcus gurneyi GFP’, and ‘Aequorea GFP’ claimed in Claims 34-36, 45 has no clear support in the specification and the claims as originally filed. The specification has not disclosed the different types of GFP or the source of GFP. The subject matter claimed in claims 34-36 and 45 broadens the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

12. Claims 18, 23, 32, and 34-36, 45 (different types of GFP) rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

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application was filed, had possession of the claimed invention. This is written description rejection.

The instant claim 18 recites an expression vector comprising HBEGF, GFP, IRES, and 2a site and CD9 site.

Claims 21 recites an expression vector comprising HBEGF (either first or second selection gene), a second selection gene, and IRES site and CD9 site.

Claim 32 recites an expression vector comprising HBEGF (either first or second selection gene) (claim 21) or HBEGF (claim 28), a second selection gene, (claim 21, claim 30), IRES, CD9 site, and another additional drug resistance selection gene.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The specification discloses several expression vectors. The specification in figures specifically in figure 18 depicts the expression vectors of the instantly claimed invention. The specification has not disclosed the combination of the expression vectors as claimed in the instant claims. The specification has not shown in possession of the claimed expression vectors. Additionally, the specification disclosure of the use of different selectable genes and disclosure of CD9 is simply not adequate support to show possession of the claimed expression vectors. The specification has not shown the combination of different selectable marker genes (GFP, HBEGF, CD9, and drug resistance gene marker combination). And further the specification has not shown different GFP species obtained from *Renilla mulleri*, *Ptilosarcus gurneyi*, and *Aequorea*. The disclosure is neither representative of the claimed genus, nor does it represent a

substantial portion of the claimed genus. Moreover, the claimed genus encompasses members, which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

Claim Objections

13. Claim 34 is objected to because of the following informalities: claim 34 recites ‘Renill Mulleri’ which is supposed to be “Renilla mulleri”. Appropriate correction is required.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claim 28 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,613,563 B1 (SOSNOWSKI et al).

The instant claim 28 recites an expression vector comprising a nucleic acid encoding HBEGF, an IRES site and a promoter of interest.

Sosnowski et al teach viral vectors with modified tropism. The reference teaches adenovirus vectors comprising a targeting ligand. The reference teaches that the targeting ligand can be heparin binding growth factors, and heparin binding EGF like factor (HBEGF) (refers to

the nucleic acid encoding HBEGF of the instant claims) (e.g., see column 11, column 22). The reference teaches heparin-binding epidermal growth factors (HBEGF) and DNA encoding HBEGF (e.g., see column 28). The reference teaches that the DNA sequence of the ligand is generally introduced into a plasmid in operative linkage with an appropriate promoter (refers to the promoter of interest of the instant claims) (e.g., see column 46). The reference teaches that in addition to the promoter internal ribosome binding site (IRES of the instant claims) (e.g., see column 49). The reference clearly anticipates the claimed invention.

16. Claims 13-32, 37-44 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,465,253 B1 (WICKHAM et al).

The instant claims briefly recite expression vector comprising HBEGF gene and a second selection gene (GFP in independent claims 13 and 25).

Wickham et al teach vectors and methods for gene transfer to cells. The reference teaches modified adenovirus vectors comprising non-native amino acid sequences. The reference teaches non-native amino acid sequence of UTV or Universal Transfer Vector sequences. The reference preferably teaches the non-native amino acid sequence or UTV sequence comprises heparin binding motifs, and a stretch of 21 amino acids of the heparin binding epidermal growth factor like growth factor (HB-EGF) (refers to the HBEGF of the instant claims). The reference teaches adenoviral vectors, which can comprise additional sequences, a protease recognition sequence (refers to 2a site of the instant claims) (e.g., see column 17). The reference teaches that the vectors comprise additional marker genes such as gene encoding GFP (refers to the second selection gene or GFP of the instant claims) (e.g., see column 19). The reference teaches that the

non-coding sequences include promoter sequences. Thus the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. Claims 13-33, 37-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over publication No. US 2002/0168649 A1 (Ferrick et al). (NOTE the publication No 2002/0168649 A1 claims priority to 09/076,624 filed on 5/12/98) and US Patent 6,465,253 B1 (WICKHAM et al).

Wickham et al teach vectors and methods for gene transfer to cells. The reference teaches modified adenovirus vectors comprising non-native amino acid sequences. The reference teaches non-native amino acid sequence of UTV or Universal Transfer Vector sequences. The reference preferably teaches the non-native amino acid sequence or UTV sequence comprises heparin binding motifs, and a stretch of 21 amino acids of the heparin binding epidermal growth factor like growth factor (HB-EGF) (refers to the HBEGF of the instant claims). The reference teaches adenoviral vectors, which can comprise additional sequences, a protease recognition sequence (refers to 2a site of the instant claims) (e.g., see column 17). The reference teaches that the vectors comprise additional marker genes such as gene encoding GFP (refers to the second

selection gene or GFP of the instant claims) (e.g., see column 19). The reference teaches that the non-coding sequences include promoter sequences.

The claimed invention differs from the prior art teachings by reciting expression vectors comprising IL-4 ε promoter. Wickham et al teach modified vectors comprising non coding sequences comprising HBEGF sequence, GFP, additional marker genes and promoter sequences. Wickham et al do not teach IL-4 ε promoter.

Ferrick et al teach candidate bioactive agents comprising a fusion nucleic acid. The fusion nucleic acid comprises an IL-4 inducible ε promoter (refers to the promoter of the instant claims) (e.g., see page 3, left column) and at least one reporter gene. The reference teaches that the reporter gene includes green fluorescent protein (GFP) (a second reporter gene or GFP of the instant claims) (e.g., see page 3, right column). The reference teaches that the IL-4 ε promoter is hooked to a second reporter gene, a death gene that may be epidermal growth factor receptor (e.g., see left column in page 4). The reference teaches that the death gene is hooked to the GFP using either IRES site or protease cleavage site (refers to IRES site and 2a site) (e.g., see right column in page 4). The reference teaches that in addition to promoter of interest, such as IL-4 ε promoter and reporter gene, the fusion nucleic acids comprises additional components including other reporter genes (refers to the additional selection genes of the instant claims), protein cleavage sites, IRES sites (e.g., see page 6, right column). The reference teaches that the exogenous constructs , which may in the form of an expression vector are retroviral vectors. The reference in figures 5B and 5C depict the disclosed constructs. The reference teaches that the compositions (the vectors) with IL-4 ε promoter are useful in high throughput screening immuno assays.

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the IL-4 ε promoter taught by Ferrick et al with the teachings of Wickham et al because Ferrick et al teach the reporter gene can be epidermal growth factor and Wickham et al teach expression vectors with HBEGF. A person skilled in the art would have been motivated to combine the teachings of Ferrick et al with Wickham et al because the advantages of the use of IL-4 ε promoter in expression vectors.

Conclusion

19. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
01 April 2004



PADMASHRI PONNALURI
PRIMARY EXAMINER